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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/712,672	11/13/2003	James McSwiggen	MBHB00-882-I (400/118)	6387

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EXAMINER	
EPPS FORD, JANET L	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 02/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/712,672	MCSWIGGEN ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-5 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-5 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 11-13-2003.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

2. Claims 1-2 and 4-5 are rejected under 35 U.S.C. 102(e) as being anticipated by Cech et al. (US Patent No. 6,444,650).

3. Claim 1 is drawn to a ribonucleic acid molecule of about 21 nucleotides in length comprising nucleotide sequence complementary to RNA sequence of telomerase reverse transcriptase (TERT) gene, wherein said ribonucleic acid molecules comprises at least one 2'-sugar modification. **Note that the instant claim does not recite the length of the nucleotide sequence that is complementary to "RNA sequence of telomerase reverse transcriptase". Additionally, the claim does not require that the ribonucleic acid molecule be fully complementary to RNA sequence of the TERT gene.

Morever, the phrase "about 21 nucleotides in length," is interpreted as encompassing ribonucleic acid molecules that are less than or greater than 21 nucleotides in length. The dependent claims are further drawn to the following limitations: (claim 2) wherein said ribonucleic acid comprises at least one phosphate backbone modification; (claim 4) wherein said ribonucleic acid molecule is single-stranded; (claim 5) wherein said sugar modification is 2'-amino, 2'-C-ally, 2'-fluoro, 2'-O-methyl, 2'-H, or any combination thereof.

Cech et al. describe ribozymes comprising 5' and 3' terminal sequences complementary to hTRT (human telomerase reverse transcriptase, see col. 3, lines 32-36) mRNA (see col. 8, lines 39-50). The ribozymes of Cech et al. include those having cleavage sites such as GUA, GUU, and GUC (see col. 8, lines 51-52). Cech et al. also teach (see Col. 9, starting at line 21) antisense nucleic acids (DNA, RNA, modified, analogues, and the like) can be made using any suitable method for producing a nucleic acid, such as the chemical synthesis and recombinant methods disclosed herein and known to one of skill in the art. In one embodiment, for example, antisense RNA that hybridizes to hTRT mRNA can be made by inserting (ligating) an hTRT DNA sequence in reverse orientation operably linked to a promoter in a vector (e.g., plasmid). Provided that the promoter and, preferably termination and polyadenylation signals, are properly positioned, the strand of the inserted sequence corresponding to the noncoding strand will be transcribed and act as an antisense oligonucleotide of the invention.

Cech et al. also provides hTRT antisense polynucleotides (RNA, DNA or modified) that can be produced by direct chemical synthesis. Chemical synthesis is

generally preferred for the production of oligonucleotides or for oligonucleotides and polynucleotides containing nonstandard nucleotides (e.g., probes, primers and antisense oligonucleotides). Chemical synthesis typically produces a single stranded oligonucleotide. It will be appreciated that the hTRT polynucleotides and oligonucleotides of Cech et al. can be made using nonstandard bases (e.g., other than adenine, cytidine, guanine, thymine, and uridine) or nonstandard backbone structures to provide desirable properties (e.g., increased nuclease-resistance, tighter-binding, stability or a desired T_M). Techniques for rendering oligonucleotides nuclease-resistant are well known in the art, a wide variety of useful modified oligonucleotides may be produced, including oligonucleotides having a peptide-nucleic acid (PNA) backbone or incorporating 2'-O-methyl ribonucleotides, phosphorothioate nucleotides, methyl phosphonate nucleotides, phosphotriester nucleotides, phosphorothioate nucleotides, phosphoramidates. Still other useful oligonucleotides may contain alkyl and halogen-substituted sugar moieties comprising one of the following at the 2' position, including the following:

> **OH, SH, SCH_3, F, OCN, OCH_3OCH_3, $OCH_3O(CH_2)_nCH_3$, $O(CH_2)_nNH_2$ or $O(CH_2)_nCH_3$, where n is from 1 to about 10; C_1 to C_{10} lower alkyl, substituted lower alkyl, alkaryl or aralkyl; Cl; Br; CN; CF_3; OCF_3; O-, S-, or N-alkyl; O-, S-, or N-alkenyl; $SOCH_3$; SO_2CH_3; ONO_2; NO_2; N_3; NH_2; heterocycloalkyl; heterocycloalkaryl; aminoalkylamino;**

The 2' modifications of the antisense nucleic acid (including RNA) encompass the modifications recited in claim 5, including 2'-amino, 2'-C-ally, 2'-fluoro, and 2'-O-methyl.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cech et al. in view of Matulic-Adamic et al. US Patent No. 6,586,238 ('238).

6. Claim 3, depends from claim 1, recites wherein said ribonucleic acid comprises a cap structure at the 5'-end, or 3'-end, or both.

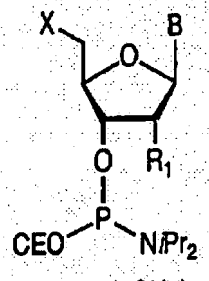
7. Cech et al. describe ribozymes comprising 5' and 3' terminal sequences complementary to hTRT (human telomerase reverse transcriptase, see col. 3, lines 32-36) mRNA (see col. 8, lines 39-50). The ribozymes of Cech et al. include those having cleavage sites such as GUA, GUU, and GUC (see col. 8, lines 51-52).

8. The discussion of Cech et al. as set forth above is incorporated here. However, Cech et al. do not teach wherein the disclosed ribonucleic acid molecules comprise the modifications recited in claim 3.

9. Matulic-Adamic, et al. ('238) teach the incorporation of chemical modifications at the 5' and/or 3' ends of nucleic acids, which are particularly useful for enzymatic cleavage of RNA or single-stranded DNA. These terminal modifications are termed as either a 5'-cap or a 3'-cap depending on the terminus that is modified. Certain of these modifications protect the enzymatic nucleic acids from exonuclease degradation. Resistance to exonuclease degradation can increase the half-life of these nucleic acids

inside a cell and improve the overall effectiveness of the enzymatic nucleic acids. These terminal modifications can also be used to facilitate efficient uptake of enzymatic nucleic acids by cells, transport and localization of enzymatic nucleic acids within a cell, and help achieve an overall improvement in the efficacy of ribozymes in vitro and in vivo. The '238 patent (see Background) also teaches that hammerhead ribozymes with terminal phosphorothioate linkages can increase resistance against cellular exonucleases. In the summary of the invention it states: The term "chemical modification" as used herein refers to any base, sugar and/or phosphate modification that will protect the enzymatic nucleic acids from degradation by nucleases. Non-limiting examples of some of the chemical modifications and methods for their synthesis and incorporation in nucleic acids are described in FIGS. 7, 8, 11-16 and infra. Some exemplary modifications are described in for example figure 7A:

FIG. 7A.



X = H, alkyl, MMTrNH-alkyl, DMTO-alkyl, Hal, $CHal_3$, NHMMTr, NHR, NR_2, NO_2, $CONH_2$, COOR, STr, SR-alkyl, OR, N_3, ONHR, or ONR_2
B = Natural bases, Modified bases or H
R_1 = H, O-Alkyl, C-Alkyl, TBDMSi, Hal, NHR (R = protecting group), or OCH_2SCH_3

These modifications encompass the specifically claimed modifications as recited in instant claim 5, including 2'-amino, 2'-C-ally, 2'-fluoro, 2'-O-methyl, and 2'-H.

It would have been obvious at the time of the instant invention to modify the ribonucleic acid (antisense or ribozyme) targeting TERT (or hTRT) of Cech et al. with the modifications disclosed by Matulic-Adamic et al. One of ordinary skill in the art at the time of the instant invention would have been motivated to make these modifications since the modifications of Matulic-Adamic et al. function to increase the nuclease resistance of modified ribozymes and protect them from degradation thereby increasing the half-life of these nucleic acids inside a cell and improve the overall effectiveness of the enzymatic nucleic acids. One of ordinary skill in the art would have had a high expectation of success for making these modifications since the teachings of Matulic-Adamic et al. are specifically drawn to the modification of ribonucleic acid.

Therefore, the invention as a whole is *prima facie* obvious over Cech et al. in view of Matulic-Adamic et al.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 9:30 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on 517-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Janet L. Epps-Ford
Primary Examiner
Art Unit 1633

JLE